Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-4. (canceled)

5. (currently amended) A method of diagnosing hepatocellular carcinoma in a human patient, comprising:

(a) detecting the level of expression in a tissue sample of two or more genes from Tables 3A, 3B, 5, 7A, 7B, 8A and 8B [3-9]; wherein differential expression of the genes in Tables 3A, 3B, 5, 7A, 7B, 8A and 8B [3-9] is indicative of hepatocellular carcinoma.

6. (currently amended) A method of detecting the progression of hepatocellular carcinoma in a human patient, comprising:

(a) detecting the level of expression in a tissue sample of two or more genes from Tables 3A, 3B, 5, 7A, 7B, 8A and 8B [3-9]; wherein differential expression of the genes in Tables 3A, 3B, 5, 7A, 7B, 8A and 8B [3-9] is indicative of hepatocellular carcinoma progression.

7. (currently amended) A method of monitoring the treatment of a human patient with hepatocellular carcinoma, comprising:

(a) administering a pharmaceutical composition to the patient;

(b) preparing a gene expression profile from a cell or tissue sample from the patient; and

(c) comparing the patient gene expression profile to a gene expression from a cell population comprising normal liver cells or to a gene expression profile from a cell population comprising hepatocellular carcinoma cells or to both.

8. (canceled)

9. (currently amended) A method of diagnosing a metastatic liver [tumor] cancer in a human patient, comprising:

(a) detecting the level of expression in a tissue sample of two or more genes from Tables 4A, 4B, 5, 6A, 6B, 9A and 9B [3-9]; wherein differential expression of the genes in Tables 4A, 4B, 5, 6A, 6B, 9A and 9B [3-9] is indicative of metastatic liver cancer.

10. (currently amended) A method of detecting the progression of a metastatic liver cancer in a human patient, comprising:

(a) detecting the level of expression in a tissue sample of two or more genes from Tables 4A, 4B, 5, 6A, 6B, 9A and 9B [3-9]; wherein differential expression of the genes in Tables 4A, 4B, 5, 6A, 6B, 9A and 9B [3-9] is indicative of a metastatic liver cancer progression.

11. (currently amended) A method of monitoring the treatment of a human patient with a metastatic liver cancer, comprising:

(a) administering a pharmaceutical composition to the patient;

(b) preparing a gene expression profile from a cell or tissue sample from the patient; and

(c) comparing the patient gene expression profile to a gene expression from a cell population comprising normal liver cells or to a gene expression profile from a cell population comprising metastatic liver tumor cells or to both.

12. (canceled)

13. (currently amended) A method of differentiating metastatic liver cancer from hepatocellular carcinoma in a human patient, comprising:

(a) detecting the level of expression in a tissue sample of two or more genes from Tables 3-9; wherein differential expression of the genes in Tables 3-9 is indicative of metastatic liver cancer rather than hepatocellular carcinoma.

14 – 46. (canceled)

47. (currently amended) A method of claim [1] 5 or 9, wherein the level of expression of 5 or more genes from [Tables 3-9] one or more tables selected from the group consisting of Tables 3A, 3B, 4A, 4B, 5, 6A, 6B, 7A, 7B, 8A, 8B, 9A and 9B is detected.

48. (currently amended) A method of claim [1] 5 or 9, wherein the level of expression of 10 or more genes from [Tables 3-9] one or more tables selected from the group consisting of Tables 3A, 3B, 4A, 4B, 5, 6A, 6B, 7A, 7B, 8A, 8B, 9A and 9B is detected.

49. (currently amended) A method of claim [1] 5 or 9, wherein the level of expression of 100 or more genes from [Tables 3-9] one or more tables selected from the group consisting of Tables 3A, 3B, 4A, 4B, 5, 6A, 6B, 7A, 7B, 8A, 8B, 9A and 9B is detected.

50. (currently amended) A method of claim [1] 5 or 9, wherein the level of expression is compared to the gene information in [Tables 3-9] one or more tables selected from the group consisting of Tables 3A, 3B, 4A, 4B, 5, 6A, 6B, 7A, 7B, 8A, 8B, 9A and 9B.

51. (currently amended) A method of diagnosing [liver cancer] hepatocellular carcinoma or metastatic liver cancer in a human patient comprising:

(a) preparing a gene expression profile from a tissue sample; and

(b) comparing the gene expression profile to a database comprising part of the data in Tables 3-9.

52. (previously presented) A method of claim 51, wherein the cancer is hepatocellular carcinoma.

53. (currently amended) A method of claim 51, wherein the cancer is metastatic [lung] liver cancer.

54. (canceled)

55. (previously presented) A method of claim 51, wherein the database comprises all of the data from Tables 3-9.

56. (canceled)

57. (previously presented) A method of claim 51, wherein the database comprises gene expression information for all of the genes from Tables 3-9.

58. (new) A method of diagnosing hepatocellular carcinoma in a human patient, comprising:

(a) detecting the level of expression in a liver tissue sample of two or more mRNA species from Table 3A, 3B, 5, 7A, 7B, 8A or 8B; and

(b) comparing the detected level of expression to the level of expression of said two or more mRNA species in a hepatocellular carcinoma liver tissue sample, thereby diagnosing hepatocellular carcinoma in the patient.

59. (new) A method of diagnosing metastatic liver cancer in a human patient, comprising:

(a) detecting the level of expression in a liver tissue sample of two or more mRNA species from Table 4A, 4B, 5, 6A, 6B, 9A or 9B; and

(b) comparing the detected level of expression to the level of expression of said two or more mRNA species in a metastatic liver cancer tissue sample, thereby diagnosing metastatic liver cancer in the patient.

60. (new) A method of claim 58, wherein the level of expression of said 2 or more mRNA species in a hepatocellular carcinoma liver sample is in Table 3A, 3B, 5, 7A, 7B, 8A or 8B.

61. (new) A method of claim 59, wherein the level of expression of said 2 or more mRNA species in a metastatic liver cancer sample is in Table 4A, 4B, 5, 6A, 6B, 9A or 9B.

REMARKS

Applicants respectfully submit that no prohibited new matter has been introduced by the foregoing amendments. Claims 5-7, 9-11, 13 and 47-53, 55 and 57-61 are pending before the Examiner for examination. Claims 1-3, 54 and 56 are presently canceled, claims 5-7, 9-11, 13, 47-51 and 53 are presently amended, and claims 58-61 have been added. Support for the amended claims can be found throughout the specification and in the original claims. Specifically, support for amended claim 9 can be found on page 20, lines 9-19 (use of the genes in Tables 3-9 to diagnose metastatic liver cancer), while support for amended claim 53 can be found on page 20, lines 9-30 (methods of diagnosing and monitoring metastatic liver cancer), page 24, lines 10-26 (analysis of liver tissue samples, normal tissue vs. metastasized cancerous tissue) and page 28, line 1, through page 30, line 13 (comparison of gene expression profiles between normal liver tissue and metastatic cancerous liver tissue). Support for amended claims 5-7, 9-11, 13 and 51 (methods of diagnosing, monitoring the progression of or monitoring the treatment of metastatic liver cancer or hepatocellular carcinoma in human patients, and a method of differentiating metastatic liver cancer from hepatocellular carcinoma in a human patient) are supported on page 24, lines 11-26, page 25, lines 23-24 and in Table 1. Claims 47-50 have been amended so that dependent claims do not depend from canceled independent claims and to recite more clearly the location of gene expression information associated with the liver cancers recited in the claims. These amended claims are supported by Tables 3A, 3B, 4A, 4B, 5, 6A, 6B, 7A, 7B, 8A, 8B, 9A and 9B. Support for claims 58-61 can be found on page 20, lines 9-19, and page 24, line 27, to page 28, line 20 (diagnosing hepatocellular carcinoma or metastatic liver cancer by comparing expression levels of two or more mRNA species in Tables 3-9 to the expression levels of these mRNA species in a liver tissue sample and preparation of mRNA species, respectively).

The Office Action dated June 3, 2003 has been carefully reviewed and the following response is made in response thereto. In view of the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

I. Summary of the Office Action

1. The Office Action rejected claims 54, 56 and 57 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as their invention.

2. The Office Action rejected claims 1-3, 5-7, 9-11, 13 and 47-57 under 35 U.S.C. §101 for lacking patentable utility due to the invention not being supported by either specific and/or substantial utility or a well established utility.

3. The Office Action rejected claims 1-3, 5-7, 9-11, 13 and 47-57 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

II. Response to the Office Action

Rejection of claims 54, 56 and 57 under 35 U.S.C. §112, second paragraph

The Office Action alleges that claims 54, 56 and 57 are indefinite for reciting the phrase "substantially all." Respectfully, "substantially all" does not appear in claim 57. With respect to claims 54 and 56, these claims have been canceled. The rejections are, therefore, moot, and Applicants request that the rejections under 35 U.S.C. §112, second paragraph be withdrawn.

Rejection of claims 1-3, 5-7, 9-11, 13 and 47-57 under 35 U.S.C. §101

The Office Action alleges that claims 1-3, 5-7, 9-11, 13 and 47-57 lack patentable utility because the invention is not supported by either specific and/or substantial utility or a well established utility. Claims 1-3, 54 and 56 have been canceled, rendering these rejections moot. The remaining claims, 5-7, 9-11, 13, 47-53, 55 and 57-61, recite methods of diagnosing metastatic liver cancer or hepatocellular carcinoma, methods of detecting the progression of metastatic liver cancer or hepatocellular carcinoma, methods of monitoring the treatment of metastatic liver cancer or hepatocellular carcinoma, and a method of differentiating metastatic liver cancer from hepatocellular carcinoma. The need for the claimed methods is discussed on pages 1 and 2 of the specification, the procedures for carrying out the claimed methods are described on pages 24-27, and the data obtained and compiled from these methods are described and analyzed in Tables 1-9 and on pages 27-34. As a result, the utility of the claimed methods is specific and clear.

The Office Action notes, on the bottom of page 3 and the top of page 4, that the genes in Tables 3-9 may be used for a variety of purposes, and these uses are disclosed in the specification. Applicants note that the list of purported uses appears to be a standard paragraph from an unrelated Office Action and not derived from the instant specification. Respectfully, there can be no doubt as